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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,808	02/06/2004	Richard Apodaca	ORT1492	8466

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PHILIP S. JOHNSON  
JOHNSON & JOHNSON  
ONE JOHNSON & JOHNSON PLAZA  
NEW BRUNSWICK, NJ 08933-7003

EXAMINER

HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 02/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/773,808

Applicant(s)

APODACA ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 November 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 4,5 and 24-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

1. Claims 1-34 are pending.

### *Election/Restrictions*

2. In response to the restriction requirement, Applicant has elected with traverse the invention of Group I, claims 3, 13-15, 20-22 and claims 1, 2, 6-12, 16-19, 23 in part, drawn to a compound wherein  $a=1$ ,  $b=0$ , and the composition thereof.

Claims of Groups II-XI are withdrawn from further consideration as being drawn to the non-elected inventions.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a. Claim 1,
  - The meaning of 'C<sub>1-5</sub> heterocyclyl', 'C<sub>3-6</sub> heterocyclyl' is unclear since the definition for these groups are not found in the specification. The scope of these groups is not clear, especially when the number, the specific heteroatoms, and the size of the rings are not described for these heterocyclyl ring systems.
  - What is a C<sub>7-12</sub> fused bicyclyl? A definition is not found in the specification wherein only bicyclic heterocyclic group is described on page 12. The scope of these groups is not clear, especially when the number, the specific heteroatoms, and the size of the rings are not described in the claim.

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- b. Claim 18, the last compound, which has no Z substituent on the phenyl, has no antecedent basis in the base claim 1.
- c. Claim 19, the first and the last compounds, which have no zsubstituent on the phenyl of Z, have no antecedent basis in the base claim 1.
- d. Claim 20, the first three and the 7<sup>th</sup> compounds, which have no heterocyclyl substituent on the phenyl, have no antecedent basis in the base claim 1.
- e. Claim 22, the first two compounds, which have no Z substituent on the phenyl<sup>3</sup>, have no antecedent basis in the base claim 1.

*The above compounds in b-e are only partial lists. Applicant is requested to check the species compounds of claims 18-22 for antecedent basis in the base claim 1.*

#### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-17, 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the compounds of claims 18-22, does not reasonably provide enablement for making and using the compounds as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant invention is drawn to a octahydroindolizine histamine H3 receptor binding compound. The preparation of example compounds has been described. The example compounds are limited to compounds wherein R11, R12, R13, R14 are H, the ring moiety in R1, R2 or R3 is phenyl.

Starting material and the process of making the instantly claimed compounds other than the example compounds, especially those wherein the substituents, such as C<sub>1-5</sub>heterocyclyl, are

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not fully described, are not seen but required. Sources are particularly pertinent because absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210 USPQ 689.

The scope of the claims therefore does not commensurate with that of the objective enablement. Since insufficient teaching and guidance are provided in the specification one of ordinary skill in the art, even with high level of skill, would not be able to make all the compounds as claimed without undue experimentation.

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 6-9, 11, 16, 17, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Carmosin I (4683239, PTO-1449). The compounds of Examples 1c, d, e, 2, 4, 9, 10, 11, 12f, and the composition thereof, are encompassed by the instant claims.

7. Claims 1-3, 6, 7, 16, 17, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Carmosin II (4689329, PTO-1449). The compound of Example 8, and the composition thereof, are encompassed by the instant claims.

***Claim Rejections - 35 USC § 103***

8. Claims 1-3, 6, 7, 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carmosin (4683239, PTO-1449).

Carmosin generically discloses an octahydroindolizine compound for treating pain (column 2). Specific compounds are described (column 3, line 32 to column 4, line 10), the

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pharmaceutically acceptable salts and optical isomers thereof, are also contemplated by Carmosin (column 4, lines 11-30).

Carmosin's N-[4[[4-octahydro-3-indoliziny]phenylthio]phenyl]-acetamide (Example 1, c, d,e) has a 4-acetamide instead of the 4-carboxy on the phenyl as recited in the last compound of instant claim 18. However, Carmosin teaches that acetamide and carboxy are optional choices (column 2, lines 24-25, definition of R1). At the time of the invention, one of ordinary skill in the art would be motivated to replace the acetamide with the alternative carboxy to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for treating pain since Carmosin had clearly taught that any species within the disclosed genus would be effective as an analgesic.

Carmosin's N-[4[4- trans-octahydro-3-indoliziny]phenyloxy]phenyl]-acetamide (Example 1c, d, e) has a 4-acetamide instead of the 4-amino on the phenyl as recited in the 6<sup>th</sup> compound of instant claim 19. However, Carmosin teaches that acetamide and amino are optional choices (column 2, lines 24-25, definition of R1). Amino as R1 is exemplified in Example 10. At the time of the invention, one of ordinary skill in the art would be motivated to replace the acetamide with the alternative amino to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for treating pain since Carmosin had clearly taught that any species within the disclosed genus would be effective as an analgesic.

Carmosin's trans-octahydro-3-[4-phenylmethoxyphenyl]-indolizine (Example 3b) has a methoxy instead of the oxy linking the two phenyls as recited in the second and third compounds in instant claim 20. However, Carmosin teaches that methoxy and oxy are optional choices (column 2, lines 19-21, definition of Q). At the time of the invention, one of ordinary skill in the art would be motivated to replace the methoxy with the alternative oxy to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for treating pain since Carmosin had clearly taught that any species, and the isomers thereof, within the disclosed genus would be effective as an analgesic.

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Carmosin's N-[4[[4-trans-octahydro-3-indoliziny]phenoxy]phenyl]-acetamide (Example 11f) has a 4-acetamide instead of the 4-amino on the phenyl as recited in the 3<sup>rd</sup> compound of instant claim 21. However, Carmosin teaches that acetamide and amino are optional choices (column 2, lines 24-25, definition of R1). Amino as R1 is exemplified in Example 10. At the time of the invention, one of ordinary skill in the art would be motivated to replace the acetamide with the alternative amino to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for treating pain since Carmosin had clearly taught that any species within the disclosed genus would be effective as an analgesic.

Carmosin's trans-3-[4-[4-chlorophenyl]thio]phenyl]-octahydro-indolizine (Example 8a) has a thio instead of the methylene linking the two phenyls as recited in the 2<sup>nd</sup> compound of instant claim 22. However, Carmosin teaches that thio and methylene are optional choices (column 2, lines 19-21, definition of Q). At the time of the invention, one of ordinary skill in the art would be motivated to replace the thio with the alternative methylene to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for treating pain since Carmosin had clearly taught that any species within the disclosed genus would be effective as an analgesic.

### ***Information Disclosure Statement***

9. The PCT search report as indicated in the PTO-1449 is not in the file, please resubmit with the next response.

### ***Conclusion***

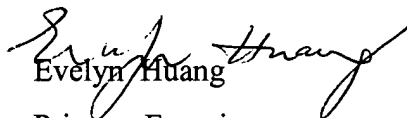
10. No claims are allowed.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Evelyn Huang

Primary Examiner

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